

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Currently Amended) A bacteriochlorophyll derivative containing at least one, preferably two or three, negatively charged groups ~~and/or~~ acidic groups that are converted to negatively charged groups at the physiological pH, or both, excluding pentacyclic bacteriochlorophyll derivatives having a free  $\text{CH}_2\text{CH}_2\text{COOH}$  or a  $\text{CH}_2\text{CH}_2\text{COO}^-$  group at position 17, and tetracyclic bacteriochlorophyll derivatives devoid of a central metal atom and having a  $-\text{CH}_2\text{CH}_2\text{COOH}$  group at position 17, a  $-\text{CH}_2\text{COOH}$  or  $-\text{COOH}$  group at position 15, a  $-\text{COOH}$  group at position 13, methyl groups at the positions 2, 7, 12, 18, and ethyl groups at the positions 3 and 8.

2. (Original) A bacteriochlorophyll derivative according to claim 1 containing two negatively charged groups.

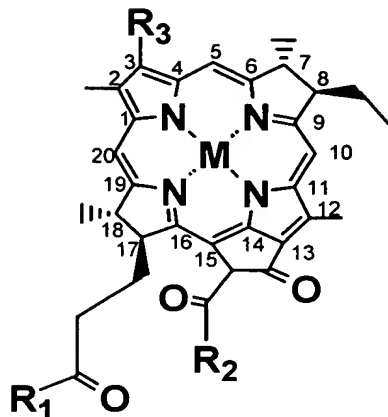
3. (Original) A bacteriochlorophyll derivative according to claim 1 containing three negatively charged groups.

4. (Currently Amended) A bacteriochlorophyll derivative according to ~~any one of claims 1 to 3~~ wherein said at least one negatively charged groups ~~are~~is selected from the group consisting of  $\text{COO}^-$ ,  $\text{COS}^-$ ,  $\text{SO}_3^-$ , and ~~or~~  $\text{PO}_3^{2-}$ .

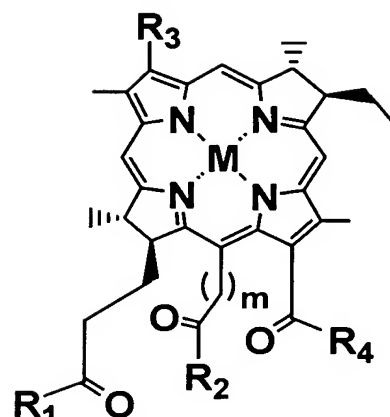
5. (Currently Amended) A bacteriochlorophyll derivative according to claim 1 wherein said at least one acidic groups that ~~are~~is converted to a negatively charged groups at the physiological pH ~~are~~is selected from the group consisting of  $\text{COOH}$ ,  $\text{COSH}$ ,  $\text{SO}_3\text{H}$ , and ~~or~~  $\text{PO}_3\text{H}_2$ .

6. (Currently Amended) A bacteriochlorophyll derivative according to ~~any one of claims 1 to 5~~ derived from a natural or synthetic derivative of bacteriochlorophyll, including compounds in which the central Mg atom has been deleted or replaced by other metal atoms.

7. (Currently Amended) A bacteriochlorophyll derivative according to claim 1 of the formula I or II:



(I)



(II)

wherein

M represents 2H or a metal atom selected from the group consisting of divalent Pd, Pt, Co, Sn, Ni, Cu, Zn and Mn, and trivalent Fe, Mn and Cr;

R<sub>1</sub>, R<sub>2</sub>, and R<sub>4</sub> each independently is Y- R<sub>5</sub>;

Y is O, S or NR<sub>5</sub>R<sub>6</sub> -NR<sub>6</sub>;

R<sub>3</sub> is selected from the group consisting of -CH=CH<sub>2</sub>, -C(=O)-CH<sub>3</sub>, -C(=O)-H, -CH=NR<sub>7</sub>, -C(CH<sub>3</sub>)=NR<sub>7</sub>, -CH<sub>2</sub>-OR<sub>7</sub>, -CH<sub>2</sub>-SR<sub>7</sub>, -CH<sub>2</sub>-NR<sub>7</sub>R'<sub>7</sub>, -CH(CH<sub>3</sub>)-OR<sub>7</sub>, -CH(CH<sub>3</sub>)-SR<sub>7</sub>, -CH(CH<sub>3</sub>)-NR<sub>7</sub>R'<sub>7</sub>, -CH(CH<sub>3</sub>)Hal, -CH<sub>2</sub>-Hal, -CH<sub>2</sub>-R<sub>7</sub>, -CH=CR<sub>7</sub>R'<sub>7</sub>, -C(CH<sub>3</sub>)=CR<sub>7</sub>R'<sub>7</sub>, -CH=CR<sub>7</sub>Hal, -C(CH<sub>3</sub>)=CR<sub>7</sub>Hal, and -C≡CR<sub>7</sub>;

R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub> and R'<sub>7</sub> each independently is H or selected from the group consisting of:

(a) C<sub>1</sub>-C<sub>25</sub> hydrocarbyl optionally containing one or more heteroatoms, carbocyclic or heterocyclic moieties, and/or

optionally substituted by one or more functional groups selected from the group consisting of halogen, oxo, OH, SH, CHO, NH<sub>2</sub>, CONH<sub>2</sub>, a negatively charged group, and an acidic group that is converted to a negatively charged group at the physiological pH;

(b) a residue of an amino acid, a peptide or of a protein; and

(c) when Y is O or S, R<sub>5</sub> may further be R<sub>8</sub><sup>+</sup>;

m is 0 or 1; and

R<sub>8</sub><sup>+</sup> is H<sup>+</sup> or a cation;

provided that:

(i) at least one, preferably two, of R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub> and R'<sub>7</sub> is a hydrocarbon chain as defined in (a) above substituted by a negatively charged group or by an acidic group that is converted to a negatively charged group at the physiological pH ; or

(ii) at least one, preferably two, of R<sub>1</sub>, R<sub>2</sub>, and R<sub>4</sub> is OH, SH, O<sup>-</sup>R<sub>8</sub><sup>+</sup> or S<sup>-</sup>R<sub>8</sub><sup>+</sup>; or

(iii) at least one of R<sub>1</sub>, R<sub>2</sub>, and R<sub>4</sub> is OH, SH, O<sup>-</sup>R<sub>8</sub><sup>+</sup> or S<sup>-</sup>R<sub>8</sub><sup>+</sup> and at least one of R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub> and R'<sub>7</sub> is a hydrocarbon chain substituted by a negatively charged group or by an acidic group that is converted to a negatively charged group at the physiological pH; or

(iv) at least one of  $R_1$ ,  $R_2$ , and  $R_4$  is OH, SH,  $O^- R_8^+$  or  $S^- R_8^+$  and at least one of  $R_5$ ,  $R_6$ ,  $R_7$  and  $R'_7$  is a residue of an amino acid, a peptide or of a protein; or

(v) at least one of  $R_5$ ,  $R_6$ ,  $R_7$  and  $R'_7$  is a hydrocarbon chain substituted by a negatively charged group or by an acidic group that is converted to a negatively charged group at the physiological pH and at least one of  $R_5$ ,  $R_6$ ,  $R_7$  and  $R'_7$  is a residue of an amino acid, a peptide or of a protein;

but excluding the compounds of formula I wherein M is as defined,  $R_3$  is  $-C(=O)CH_3$ ,  $R_1$  is OH or  $OR_8^+$  and  $R_2$  is  $-OCH_3$ , and the compound of formula II wherein M is 2H,  $R_3$  is  $-C(=O)CH_3$ ,  $R_1$ ,  $R_2$  and  $R_4$  are OH, and m is 0 or 1.

8. (Currently Amended) A bacteriochlorophyll derivative of the formula I or II according to claim 7 wherein said negatively charged groups are selected from the group consisting of  $COO^-$ ,  $COS^-$ ,  $SO_3^-$ , and ~~or~~  $PO_3^{2-}$ .

9 (Currently Amended). A bacteriochlorophyll derivative of the formula I or II according to claim 7 wherein said acidic groups that are converted to negatively charged groups at the physiological pH are selected from the group consisting of COOH, COSH,  $SO_3H$ , and ~~or~~  $PO_3H_2$ .

10 (Currently Amended). A bacteriochlorophyll derivative of the formula I or II according to claim 7 wherein  $R_1$  is  $Y-R_5$ ;  $Y$  is O, S or NH; and  $R_5$  is a hydrocarbon chain substituted by functional groups selected from of the group consisting of OH, SH,  $SO_3H$ ,  $NH_2$ ,  $CONH_2$ ,  $COOH$ ,  $COSH$ , and  $PO_3H_2$ .

11. (Original) A bacteriochlorophyll derivative of the formula I or II according to claim 7 wherein  $R_5$  is the residue of an amino acid, a peptide or a protein.

12. (Currently Amended) A bacteriochlorophyll derivative of the formula I or II according to claim ~~4~~ 7 containing a central Pd metal atom.

13. (Original) A bacteriochlorophyll derivative of the formula I according to claim 7 wherein:

M is Pd;

$R_1$  is  $-NH-(CH_2)_n-SO_3^-R_8^+$ ,  $-NH-(CH_2)_n-COO^-R_8^+$ ;  $-NH-(CH_2)_n-PO_3^{2-} (R_8^+)_2$  ;

$R_2$  is methoxy;

$R_3$  is  $-C(=O)-CH_3$ ;

$R_8^+$  is a monovalent cation such as  $K^+$ ,  $Na^+$ ,  $Li^+$ ,  $NH_4^+$ ; and

$n$  is an integer from 1 to 10, preferably 2 or 3.

14. (Currently Amended) A bacteriochlorophyll derivative of the formula II according to claim 7 wherein:

M represents 2H, divalent Pd, Cu, or Zn or trivalent Mn;

$R_1$  is  $-O^-R_8^+$ ,  $-NH-(CH_2)_n-SO_3^-R_8^+$ ,  $-NH-(CH_2)_n-COO^-R_8^+$  or  $-NH-(CH_2)_n-PO_3^{2-}(R_8^+)_2$ ; or  $Y-R_5$  wherein Y is O, S or NH and  $R_5$  is the residue of an amino acid, a peptide or a protein;

$R_2$  is  $C_1-C_6$  alkoxy, ~~such as methoxy, ethoxy, propoxy, butoxy, more preferably methoxy;~~

$R_3$  is  $-C(=O)-CH_3$ ,  $-CH=N-(CH_2)_n-SO_3^-R_8^+$ ;  $-CH=N-(CH_2)_n-COO^-R_8^+$ ;  $-CH=N-(CH_2)_n-PO_3^{2-}(R_8^+)_2$ ;  $-CH_2-NH-(CH_2)_n-SO_3^-R_8^+$ ;  $-CH_2-NH-(CH_2)_n-COO^-R_8^+$ ; or  $-CH_2-NH-(CH_2)_n-PO_3^{2-}(R_8^+)_2$ ;

$R_4$  is  $-NH-(CH_2)_n-SO_3^-R_8^+$ ;  $-NH-(CH_2)_n-COO^-R_8^+$ ; or  $-NH-(CH_2)_n-PO_3^{2-}(R_8^+)_2$ ;

$R_8^+$  is a monovalent cation, ~~such as  $K^+$ ,  $Na^+$ ,  $Li^+$ ,  $NH_4^+$ , more preferably  $K^+$ ;~~ and

m is 1, and n is an integer from 1 to 10; preferably 2 or 3.

15. (Currently Amended) A bacteriochlorophyll derivative of formula II in claim 7 wherein:

M is divalent Pd;

$R_1$  is  $-O^-R_8^+$ ,  $-NH-(CH_2)_n-SO_3^-R_8^+$ , or  $Y-R_5$  wherein Y is O, S

or NH and  $R_5$  is the residue of an amino acid, a peptide or a protein;

$R_2$  is  $C_1$ - $C_6$  alkoxy, preferably methoxy;

$R_3$  is  $-C(=O)-CH_3$ ,  $-CH=N-(CH_2)_n-SO_3^- R_8^+$  ; or  $-CH_2-NH-(CH_2)_n-SO_3^- R_8^+$  ;

$R_4$  is  $-NH-(CH_2)_n-SO_3^- R_8^+$  ;  $NH-(CH_2)_n-COO^- R_8^+$  ; or  $NH-(CH_2)_n-PO_3^{2-} (R_8^+)_2$  ;

$R_8^+$  is a monovalent cation, preferably  $K^+$ ;

m is 1, and n is 2 or 3.

16. (Original) A bacteriochlorophyll derivative of the formula I according to claim 13, consisting of the compound Palladium bacteriopheophorbide a  $17^3$ -(3-sulfopropyl)amide potassium salt.

17. (Currently Amended) A bacteriochlorophyll derivative of the formula II according to claim 15, selected from the group consisting of the compounds:

Palladium  $3^1$ -oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin  $13^1$ -(2-sulfoethyl) amide dipotassium salt;

$3^1$ -oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin  $13^1$ -(2-sulfoethyl) amide dipotassium salt;

Palladium  $3^1$ -oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin  $13^1, 17^3$ -di(3-sulfopropyl)amide dipotassium salt;



Palladium 3<sup>1</sup>-(3-sulfopropylimino)-15-methoxycarbonylmethyl-rhodobacterio-chlorin 13<sup>1</sup>,17<sup>3</sup>-di(3-sulfopropyl)amide tripotassium salt;

Copper(II) 3<sup>1</sup>-oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin 13<sup>1</sup>-(2-sulfoethyl) amide dipotassium salt;

Zinc 3<sup>1</sup>-oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin 13<sup>1</sup>-(2-sulfoethyl) amide dipotassium salt;

Manganese(III) 3<sup>1</sup>-oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin 13<sup>1</sup>-(2-sulfoethyl)amide dipotassium salt;

Palladium 3<sup>1</sup>-oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin 13<sup>1</sup>-(2-sulfoethyl) amide, 17<sup>3</sup>-(N-immunoglobulin G) amide potassium salt;

Palladium 3<sup>1</sup>-oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin 13<sup>1</sup>-(2-carboxy-ethyl)amide dipotassium salt;

Palladium 3<sup>1</sup>-oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin 13<sup>1</sup>-(3-phosphopropyl)amide tripotassium salt; and

Palladium 3<sup>1</sup>-(3-sulfopropylamino)-15-methoxycarbonylmethyl-rhodobacteriochlorin 13<sup>1</sup>,17<sup>3</sup>-di(3-sulfopropyl)amide tripotassium salt.

18. (Original) Palladium 3<sup>1</sup>-oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin 13<sup>1</sup>-(2-sulfoethyl) amide dipotassium salt.

19. (Currently Amended) A pharmaceutical composition comprising a bacteriochlorophyll derivative according to ~~any one of claims 1 to 18~~, and a pharmaceutically acceptable carrier.

20. (Original) The pharmaceutical composition according to claim 19 for photodynamic therapy.

21. (Original) The pharmaceutical composition according to claim 20 for vascular-targeting photodynamic therapy.

22. (Currently Amended) The pharmaceutical composition according to claim 20 ~~or 21~~ for photodynamic therapy of tumors, including metastatic tumors.

23. (Original) The pharmaceutical composition according to claim 22 for photodynamic therapy of melanoma, colon, breast, lung, or prostate cancer.

24. (Currently Amended) The pharmaceutical composition according to claim 20 ~~or 21~~ for photodynamic therapy of age-related macular degeneration.

25. (Currently Amended) The pharmaceutical composition according to claim 20 ~~or 21~~ for photodynamic therapy of benign prostate hypertrophy.

26. (Original) The pharmaceutical composition according to claim 19 for tumor diagnosis.

27. (Original) A pharmaceutical composition according to claim 19 for killing cells or infectious agents comprising bacteria and viruses.

28. (Original) The pharmaceutical composition according to claim 27 for *in vitro* killing of cells or infectious agents comprising bacteria and viruses in a biological product upon illumination of said product.

29. (Original) The pharmaceutical composition according to claim 28 wherein said biological product is blood.

30.-35. (Cancelled)

36. (Currently Amended) A method for tumor photodynamic therapy which comprises:

(a) administering to an individual in need a compound according to ~~any one of claims 1 to 18~~; and  
(b) irradiating the local of the tumor.

37. (Currently Amended) A method for photodynamic therapy of age-related macular degeneration which comprises:

(a) administering to an individual in need a compound according to ~~any one of claims 1 to 18~~; and (b) irradiating the local of the macular degeneration.

38. (Currently Amended) A method for tumor diagnosis which comprises:

(a) administering to a subject suspected of having a tumor, a compound according to ~~any one of claims 1 to 18~~; and

(b) irradiating the subject by standard procedures and measuring the fluorescence of the suspected area, wherein a higher fluorescence indicates tumor sites.

39 (Currently Amended). In a method for photodynamic therapy using a photosensitizer, the improvement wherein said photosensitizer is a bacteriochlorophyll derivative according to ~~any one of claims 1 to 18~~.

40. (Currently Amended) In a method for diagnosis of tumors using a photosensitizer, the improvement wherein said photosensitizer is a bacteriochlorophyll derivative, according to ~~any one of claims 1 to 18.~~

41. (Currently Amended) In an in vitro method for killing of cells or infectious agents comprising bacteria and viruses, using a photosensitizer, the improvement wherein said photosensitizer is a bacteriochlorophyll derivative according to ~~any one of claims 1 to 18.~~

42. (Original) The compound Palladium bacteriopheophorbide a  $17^3$ -(3-sulfo-1-oxysuccinimide) ester sodium salt, as an intermediate.

43. (Original) A method for the preparation of compounds of formula II In claim 7 wherein  $R_1$  is  $-O^- R_8^+$ ;  $R_2$  is  $-OCH_3$ ;  $R_3$  is acetyl;  $R_4$  is a group  $-NH-(CH_2)_n-SO_3^- R_8^+$ ;  $R_8^+$  is a monovalent cation; m is 1 and n is 1 to 10, which comprises:

(i) reacting the corresponding M-bacteriopheophorbide of formula I wherein  $R_1$  is OH with an aminosulfonic acid of the formula  $H_2N-(CH_2)_n-SO_3H$  in a  $R_8^+$ -buffer; and

(ii) isolating the desired compound of formula II.

44. (Original) The method according to claim 43 for preparation of palladium 3<sup>1</sup>-oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin 13<sup>1</sup>-(2-sulfoethyl) amide dipotassium salt which comprises: (i) reacting Pd-bacteriopheophorbide a with taurine of the formula  $\text{H}_2\text{N}-(\text{CH}_2)_2-\text{SO}_3\text{H}$  in a  $\text{K}^+$ -buffer; and (ii) isolating the title compound.

45. (Original) A method for the preparation of compounds of formula II in claim 7 wherein  $\text{R}_1$  is  $-\text{O}^- \text{R}_8^+$ ;  $\text{R}_2$  is  $-\text{OCH}_3$ ;  $\text{R}_3$  is acetyl;  $\text{R}_4$  is a group  $-\text{NH}-(\text{CH}_2)_n-\text{COO}^- \text{R}_8^+$ ;  $\text{R}_8^+$  is a monovalent cation; m is 1 and n is 1 to 10, which comprises: (i) reacting the corresponding M-bacteriopheophorbide of formula I wherein  $\text{R}_1$  is OH with an aminocarboxylic acid of the formula  $\text{H}_2\text{N}-(\text{CH}_2)_n-\text{COOH}$  in a  $\text{R}_8^+$ -buffer; and (ii) isolating the desired compound of formula II.

46. (Original) A method for the preparation of compounds of formula II in claim 7 wherein  $\text{R}_1$  is  $-\text{O}^- \text{R}_8^+$ ;  $\text{R}_2$  is  $-\text{OCH}_3$ ;  $\text{R}_3$  is acetyl;  $\text{R}_4$  is a group  $-\text{NH}-(\text{CH}_2)_n-\text{PO}_3^{2-} (\text{R}_8^+)_2$ ;  $\text{R}_8^+$  is a monovalent cation; m is 1 and n is 1 to 10, which comprises: (i) reacting the corresponding M-bacteriopheophorbide of formula I wherein  $\text{R}_1$  is OH with an aminophosphonic acid of the formula  $\text{H}_2\text{N}-(\text{CH}_2)_n-\text{PO}_3\text{H}_2$  in a  $\text{R}_8$ -buffer; and (ii) isolating the desired compound of formula II.

47. (Original) A method for the preparation of compounds of formula II in claim 7 wherein  $R_1$  and  $R_4$  contain the same negatively charged group, which comprises:

- (i) reacting the corresponding M-bacteriopheophorbide with an excess of the aminosulfonic, aminocarboxylic or aminophosphonic acid in a  $R_8^+$ -buffer; and
- (ii) isolating the desired 13,17-disubstituted derivative of formula II.

48. (Original) A method for the preparation of compounds of formula II in claim 7 wherein  $R_1$  and  $R_4$  are each a group  $-NH-(CH_2)_n-SO_3^-R_8^+$ ;  $R_2$  is  $-OCH_3$ ;  $R_3$  is acetyl;  $R_8^+$  is a monovalent cation;  $m$  is 1 and  $n$  is 1 to 10, which comprises:

- (i) coupling the corresponding M-bacteriopheophorbide of formula I wherein  $R_1$  is OH with N-hydroxy-sulfosuccinimide (sulfo NHS) in the presence of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC);
- (ii) reacting the resulting M-bacteriopheophorbide-17<sup>3</sup>-N-hydroxy-sulfosuccinimide ester with an excess of an aminosulfonic acid of the formula  $H_2N-(CH_2)_n-SO_3H$  in a  $R_8^+$ -buffer, thus obtaining a compound of formula I having a sole negatively charged group at position 17;

- (iii) reacting the product of step (ii) with an excess of  $\text{H}_2\text{N}-(\text{CH}_2)_n-\text{SO}_3\text{H}$  in a  $\text{R}_8^+$ -buffer; and
- (iv) isolating the desired compound of formula II.

49. (Original) A method for the preparation of compounds of formula II in claim 7 wherein  $\text{R}_1$  and  $\text{R}_4$  are each a group  $-\text{NH}-(\text{CH}_2)_n-\text{COO}^-\text{R}_8^+$ ;  $\text{R}_2$  is  $-\text{OCH}_3$ ;  $\text{R}_3$  is acetyl;  $\text{R}_8^+$  is a monovalent cation;  $m$  is 1 and  $n$  is 1 to 10, which comprises:

(i) coupling the corresponding M-bacteriopheophorbide of formula I wherein  $\text{R}_1$  is OH with N-hydroxy-sulfosuccinimide (sulfo NHS) in the presence of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC);

(ii) reacting the resulting M-bacteriopheophorbide-17<sup>3</sup>-N-hydroxy-sulfosuccinimide ester with an excess of an aminocarboxylic acid of the formula  $\text{H}_2\text{N}-(\text{CH}_2)_n-\text{COOH}$  in a  $\text{R}_8^+$ -buffer, thus obtaining a compound of formula I having a sole negatively charged group at position 17;

(iii) reacting the product of step (ii) with an excess of  $\text{H}_2\text{N}-(\text{CH}_2)_n-\text{COOH}$  in a  $\text{R}_8^+$ -buffer; and (iv) isolating the desired compound of formula II.

50. (Original) A method for the preparation of compounds of formula II in claim 7 wherein  $\text{R}_1$  and  $\text{R}_4$  are each a



group  $\text{-NH-(CH}_2\text{)}_n\text{-PO}_3^{2-} \text{R}_8^+$ ;  $\text{R}_2$  is  $\text{-OCH}_3$ ;  $\text{R}_3$  is acetyl;  $\text{R}_8^+$  is a monovalent cation;  $m$  is 1 and  $n$  is 1 to 10, which comprises:

(i) coupling the corresponding M-bacteriopheophorbide of formula I wherein  $\text{R}_1$  is OH with N-hydroxy-sulfosuccinimide (sulfo NHS) in the presence of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC);

(ii) reacting the resulting M-bacteriopheophorbide-17<sup>3</sup>-N-hydroxy-sulfosuccinimide ester with an excess of an aminophosphonic acid of the formula  $\text{H}_2\text{N-(CH}_2\text{)}_n\text{-PO}_3\text{H}_2$  in a  $\text{R}_8^+$ -buffer, thus obtaining a compound of formula I having a sole negatively charged group at position 17;

(iii) reacting the product of step (ii) with an excess of  $\text{H}_2\text{N-(CH}_2\text{)}_n\text{-PO}_3\text{H}_2$  in a  $\text{R}_8^+$ -buffer; and (iv) isolating the desired compound of formula II.